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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

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01/25/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,212	CASCALHO ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-28* is/are pending in the application.

4a) Of the above claim(s) *15,16,18-20,22 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,17,21 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment, filed 11/11/2010, has been entered.

Claims 1-13 and 29-32 have been canceled.

Claims 14-28 are pending.

Claims 15-16, 18-20, 22 and 28 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention/species, there being no allowable generic or linking claims. The election was made without traverse in the reply filed on 08/12/2009.

Claims 14, 17, 21 and 23-27 are currently under examination as they read on a method for increasing T cell diversity and monitoring T cell diversity in a subject.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Applicant's 132 Declaration, filed 11/11/2010, was sufficient to over come the previous rejection under 35 U.S.C. 103(a) as being unpatentable over Koduri et al. (*American Journal of Hematology* 1999, 61:16-20) in view of Urbani et al. (*Transplantation Proceedings* 2000, 32:2707-2709), Ogle et al. (US 2007/0042349 A1, citation on IDS), Song et al. (*Blood* 2003, 101:3708-3713) and Goronzy et al. (*Arthritis Res. Ther.* 2003, 5:225-234).

The following new grounds of rejection are necessitated by Applicant's remarks/declaration.

Claims 14, 17, 21, 23-27 rejected under 35 U.S.C. 103(a) as being unpatentable over Koduri et al. (*American Journal of Hematology* 1999, 61:16-20) in view of Urbani et al. (*Transplantation Proceedings* 2000, 32:2707-2709), Wagner et al. (PNAS 1998, 95:14447-14452; cited on IDS), Song et al. (*Blood* 2003, 101:3708-3713) and Pira et al. (*Immunology Letters 2001, 79:85-91*).

Koduri et al. taught a method for increasing T cell diversity in a subject comprising administering polyclonal immunoglobulins wherein said subject has AIDS (which also reads on chronic infection) and is at least 20 years old (see entire document, in particular, see Introduction and Table 1 on page 17). It is noted that the intravenous immunoglobulin (IVIG) reads on polyclonal immunoglobulin as evidenced by Song et al. (see page 3708, Introduction, first paragraph).

Although Koduri was silent on "increasing T cell diversity", it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). Given that the prior art taught the same or nearly the same method step of administering polyclonal immunoglobulins to subjects with AIDS, one of ordinary skill in the art would have recognized that the method taught by Koduri would necessarily increase T cell diversity in the subjects. The fact that Applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that

method.

Furthermore, it is also noted that the immunoglobulins in IVIG are predominantly monomers as evidenced by Song et al. (see page 3708, Introduction, first paragraph). Therefore, the limitation of "reduced monomers" is deemed a product-by-process limitation wherein said monomeric polyclonal immunoglobulins are produced by reducing process. However such process does not distinguish from the monomeric polyclonal immunoglobulins in the art. "[E]ven though product-by-process claims are limited by and defined by the process; determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Similarly, the "recombinant" limitation is also a product-by-process limitation wherein said polyclonal immunoglobulins are produced by recombinant process. However such process does not distinguish from the polyclonal immunoglobulins in the art.

Koduri did not teach said polyclonal immunoglobulins are Fab fragments. However, it would have been obvious to one of ordinary skill in the art to use Fab fragments in the IVIG treatment because Fab fragments are both easy to obtain and offer the advantage of preventing hyperacute rejection in host while maintaining its hemolytic complement activity as taught by Urbani et al. (see entire document, in particular, see e.g., Introduction and Discussion). Upon reading Urbani, one of ordinary

skill in the art would have been motivated to use Fab fragments of polyclonal immunoglobulin because Urbani taught that Fab interferes with the hyperacute xenorejection process without depleting complement, thus making it available for host defense (see page 2709, left column). Furthermore, one of ordinary skill in the art would have reasonable expectation of success to make Fab fragments of polyclonal immunoglobulin using known methods well-within his or her technical grasp, such as papain digest.

The teaching by Koduri et al. differs from the present claims in that Koduri did not teach monitoring T cell diversity in the subject. However, it would have been obvious to one of ordinary skill in the art to monitor T cell diversity in view of the teaching by Pira et al. (see entire document). In particular, Pira et al. taught that in order to monitor the cellular immune state of a HIV patient, CD4 T cells should be monitored by defining the specificity or clonal diversity (see Abstract). Upon reading the prior art, one of ordinary skill in the art would have been reasonably expected to monitor T cell diversity in subjects with HIV infection. Furthermore, it would have been obvious to one of ordinary skill would to use a population of random or diverse nucleic acid molecules to measure diversity in T cell population in view of the teaching by Wagner et al. because Wagner et al. taught monitoring T cell diversity in subjects with decrease lymphocyte diversity such as one with rheumatoid arthritis (see entire document]). In particular, Wagner et al. taught a method for determining T cell diversity in a subject using a population of random or diverse nucleic acid molecules wherein the random nucleic acid molecules

are the probes spanning the N-D-N region (page 14447, fourth paragraph; page 14448, second and third paragraph; page 14448, second and third paragraph).

Upon reading the teaching by Wagner, one of ordinary skill in the art would have been reasonably expected to use the technique to monitor T cell diversity in the treatment method taught by Koduri et al. because Koduri taught treating parvovirus B19 in patients with AIDS; Pira taught that subjects with HIV infection have decreased T cell diversity and Wagner taught using a population of random or diverse nucleic acid molecules to measure diversity in T cell population in subjects with decreased T cell diversity.

Given the above discussion, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Primary Examiner, Art Unit 1644
January 17, 2011